REMARKS/ARGUMENTS

Claims 23-24, 26, and 28-37 are currently pending in the above-identified application. By this submission, claim 23 has been amended. No new matter has been added by this amendment. Applicants respectfully request reconsideration of the claims currently pending in the application in light of the amendment above and the below remarks.

Rejections under 35 U.S.C. §102(e):

Claims 23-24, and 31-36 remain rejected under 35 U.S.C. §102(e) as being anticipated by Cohen *et al.*, for reasons already of record in paper of August 20, 2003. The Examiner has summarized Applicants' prior argument as stating that "Cohen teaches that certain undefined combinations of cytokines have been used to amplify (or partially substitute the calcium ionophore for) the activation/conversion of monocytes to activate dendritic cell-like phenotype, and that this teaching does not anticipate the present invention as no specific combination is cited." Further, the prior argument has been recited as "asserting that the term activation/conversion as used by Cohen refers to mature dendritic cells state at the conclusion of their process and that these activated cells cannot take up and process antigen." Applicants' arguments is further asserted as providing that "Cohen has compared various cytokines to be inferior to the use of calcium ionophore in converting monocytes to activiated dendritic cell-like phenotype."

The Examiner has also noted that she does not believe that the claims are limited to cytokines that consist of only GM-CSF and IL-4. It appears that because of this interpretation of the claims the Examiner continues to believe that the composition taught by Cohen *et al.* "seems to be" the same as the claimed composition, "*i.e.*, monocytes that have been exposed to a combination of cytokines comprising GM-CSF, IL-2, IL-4 and IL-12, and prostate cancer cell lysates, wherein exposure to a combination of cytokines would convert monocytes to immature dendritic cells, that could present soluble antigen, as taught by Sallusto *et al.* (abstract and p.111,first column, first paragraph), to activate specific T cells."

Applicants again must strongly disagree with the Examiner's analysis of the Cohen reference. First, Applicants have not asserted that Cohen *et al.* compared various cytokine combinations as being inferior to calcium ionophore. The statement relating to combinations of cytokines is a direct quote from the Cohen *et al.* reference. See column 10, lines 50 through 61. Second, the Examiner continues to state that the composition disclosed by Cohen *et al.* appears to be the same as that claimed by Applicants. This can not be the case if the method disclosed by Cohen *et al.* can not provide a dendritic cell population that does not increase the amount of antigen on the surface of the dendritic cells as compared to a control. It should be noted that Cohen does not disclose or suggest the addition of antigen to monocytes exposed to any combination of cytokines, but instead discloses the addition of some undefined combination of cytokines to calcium ionophore to the elutriated cell population to from the activated APC population. See for example, Table 3, step 8 (column 13)). The antigen is added to the activated APC population harvested and used to stimulate growth of T lymphocytes. As provided in prior arguments. Activated dendritic cells that have undergone the process of Cohen can not uptake and process antigen and can not form the cell population that is the subject of the pending claims.

Although Applicants do not agree with the Examiner's basis for rejection, but in order to further expedite prosecution of certain subject matter claim 23 has been amended to recite "[a] composition comprising an isolated cell population having human dendritic cells, wherein said cell population has been cultured in the presence of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 4 (IL-4), and no additional cytokine, and exposed *in vitro* to a soluble prostate antigen, the cell population having an increased ability to activate T cells specific to the prostate antigen as compared to a similar isolated cell population cultured in the presence of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 4 (IL-4), and no additional cytokine, that has not been exposed *in vitro* to the prostate antigen." This amendment is fully supported by the specification as filed, for example, at page 17, lines 25-26, page 22, lines 15-17, and through out the specification. As Cohen *et al.* do not

disclose or suggest the specific combination of cytokines in the amended claims, the reference can not anticipate the claimed invention.

Therefore, in view of the amendments and remarks above Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 23, 24, and 31-36 under 35 U.S.C. § 102, as anticipated by Cohen *et al.* as evidenced by Sallusto *et al.*

Rejections under 35 U.S.C. 103:

Claims 23-24, and 31-36 remain rejected under 35 U.S.C. §103 as being obvious over Cohen *et al.*, in view of Sallusto *et al.*, and Inaba *et al.*, for reasons already of record in paper of August 20, 2003. As above, the Examiner has stated that the claims in the present application are not limited to GM-CSF and IL-4 and that therefore the composition taught by Cohen *et al.*, monocytes exposed to a combination of cytokines that includes GM-CSF, IL-2, IL-4 and IL-12, and prostate cancer cell lysates seems to be the same as the claimed composition. The Examiner has also stated that the specific monocyte composition taught by Cohen *et al.*, which is cited in this rejection is not related to monocytes exposed to calcium ionophore.

Applicants must again strongly object to the present rejection. In particular, Applicants must respectfully question the statement or the Examiner that Cohen *et al.* disclosed monocyte compositions not related to monocytes exposed to calcium ionophore. If the Examiner is referring to the passage at column 10, lines 50-61, Applicants believe this disclosure as previously stated by Applicants in earlier responses is merely a broad summary statement of the prior work of others and comparison of the prior results to calcium ionophore treatment. What Cohen *et al.* disclose in relation to combinations of cytokines is found at lines 60 through 61 of column 10 and in Table 3, step 8 (See column 13). In this step Cohen *et al.* specifically disclose the addition of "[s]pecific recombinant cytokine combinations in some instances", including for example, "rhIL-12, rhGM-CSF, rhIL-4 and rhIL-2" with the calcium ionophore. Antigen is then added to the activated DC phenotype cells. Therefore, contrary to the position of the Examiner

Cohen *et al.* does not disclose or suggest a specific monocyte composition that is not related to monocytes exposed to calcium ionophore.

Further, the Examiner believes that one would have expected that exposure of monocytes or blood mononuclear cells to a combination of cytokines, such as GM-CSF and IL-4 would convert them to immature dendritic cells, that could efficiently present soluble antigen to activate specific T cells, as "clearly taught by Sallusto *et al.* (abstract and p 1111, first column, first paragraph)." Still further, the Examiner believes the "motivation to combine Cohen *et al.* with Sallusto *et al.* is that Sallusto *et al.* teach more details how to activate monocytes using cytokines, and that exposure of dendritic cells produced by exposure to cytokines as taught by Cohen *et al.*, or Sallusto *et al.*, to a cancer cell, such as prostate cancer cell lysates taught by Cohen *et al.* would have potential use for treating prostate cancer, because dendritic cells could efficiently present soluble antigen to activate specific T cells, as clearly taught by Sallusto *et al.*, and could reduce the size of prostate tumor, as taught by Cohen *et al.* (Example 2)."

Applicants strongly disagree with the Examiner's analysis of the motivation to combine Cohen *et al.* with Sallusto *et al.*. In particular, as above, Cohen *et al.* do not disclose a cell population that has not been exposed to calcium ionophore. Further, Sallusto *et al.* do not address tumor cell lysates or other "normal" tumor antigens and does not anticipate their use for therapeutic purposes. Therefore, Cohen *et al.* as stated in prior response teaches away from using monocyte cell populations that have been exposed only to combinations of cytokines because they were not as effective as calcium ionophore and provides a prophetic example of a treatment method that can not process and present any soluble antigen, much less a prostate tumor cell lysate.

As to Inaba *et al.*, the Examiner asserts that "in view of the teachings of Inaba *et al.* one would have expected that that it is the properties of dendritic cells taught by Cohen *et al.*, and Sallusto *et al.* to activate CD4+ and/or CD8+ T cells." Applicants do not believe this summary of the teaching of Inaba *et al.* to be correct. Inaba *et al.* teach the use of dendritic cells

to stimulate T cells, but T cell activation was only demonstrated for *ex vivo* isolated cells, not dendritic cells that have been derived from *in vitro* cultured monocytes. Furthermore, Inaba *et al.* describe the stimulation of T cells in a mixed lymphocyte reaction and does not describe the uptake or processing of any antigen much less a prostate tumor cell lysate. Also, the T cell activation measured by mixed lymphocyte reaction is a non-specific T cell activation, not an antigen specific T cell activation as required by the present claims. Still further, Inaba *et al.* state at page 192, "[o]f some interest is the role of dendritic cells in the primary response to viral and tumor antigens on other cells. Are antigens on infected or malignant cells presented directly to unprimed $CD8^+$ T lymphocytes or via a dendritic cell in the host?". Therefore, Inaba *et al.* does not appear to provide any motivation to the skilled artisan to expect that the properties of dendritic cells taught by either Cohen *et al.* or Sallusto *et al.* would activate CD4+ or CD8+ T cells.

As above, although Applicants do not agree with the Examiner's basis for rejection, but in order to further expedite prosecution of certain subject matter claim 23 has been amended to recite "[a] composition comprising an isolated cell population having human dendritic cells, wherein said cell population has been cultured in the presence of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 4 (IL-4), and no additional cytokine, and exposed *in vitro* to a soluble prostate antigen, the cell population having an increased ability to activate T cells specific to the prostate antigen as compared to a similar isolated cell population cultured in the presence of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin 4 (IL-4), and no additional cytokine, that has not been exposed *in vitro* to the prostate antigen." None of the references either alone or in any combination disclose or suggest the invention as currently claimed.

Therefore, in view of the amendments and remarks above Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 23, 24, and 31-36 under 35 U.S.C. § 102, as anticipated by Cohen *et al.* as evidenced by Sallusto *et al.*

Claim 26 remains rejected under 35 U.S.C. §103 as being obvious over Cohen *et al.*, in view of Sallusto *et al.*, and further in view of Lutz *et al.* for reasons already of record in paper of August 20, 2003. In particular, as above, the Examiner believes that the composition of dendritic cells taught by Cohen *et al.*, and Sallusto *et al.* seem to be the same as the claimed composition. As above, Applicants have demonstrated that neither Cohen *et al.* or Sallusto *et al.*, alone or in any combination, teach nor suggest the dendritic cell compositions of the present invention. Further, as above claim 23 has been amended to recite the specific cytokine combination of GM-CSF and IL-4 without additional cytokines to further expedite prosecution of a certain aspect of the present invention. Claim 26 is dependent from claim 23 and therefore encompasses all limitations from claim 23. Therefore, Lutz *et al.* adds nothing to render obvious the immortalized dendritic cells of the invention as either previously or presently claimed.

Claims 28-29 remain rejected under 35 U.S.C. §103 as being obvious over Cohen *et al.*, in view of Sallusto *et al.*, and further in view of Taylor *et al.* for reasons already of record in paper of August 20, 2003. In particular, as above, the Examiner believes that the composition of dendritic cells taught by Cohen *et al.*, and Sallusto *et al.* seem to be the same as the claimed composition. As above, Applicants have demonstrated that neither Cohen *et al.* or Sallusto *et al.*, alone or in any combination, teach nor suggest the dendritic cell compositions of the present invention. Further, as above claim 23 has been amended to recite the specific cytokine combination of GM-CSF and IL-4 without additional cytokines to further expedite prosecution of a certain aspect of the present invention. Claims 28-29 are dependent from claim 23 and therefore encompasses all limitations from claim 23. Therefore, Taylor *et al.* adds nothing to render obvious the preserved dendritic cells of the invention as either previously or presently claimed.

Claim 30 remains rejected under 35 U.S.C. §103 as being obvious over Cohen *et al.*, in view of Sallusto *et al.*, and further in view of Taylor *et al.* and Lutz *et al.*, for reasons

already of record in paper of August 20, 2003. In particular, as above, the Examiner believes that the composition of dendritic cells taught by Cohen *et al.*, and Sallusto *et al.* seem to be the same as the claimed composition. As above, Applicants have demonstrated that neither Cohen *et al.* or Sallusto *et al.*, alone or in any combination, teach nor suggest the dendritic cell compositions of the present invention. Therefore there is no motivation for the skilled artisan to combine the references as suggested by the Examiner. Further, as above claim 23 has been amended to recite the specific cytokine combination of GM-CSF and IL-4 without additional cytokines to further expedite prosecution of a certain aspect of the present invention. Claim 30 is dependent from claim 28 and claim 23 and therefore encompasses all limitations from claims 23 and 28. Therefore, the combination of Cohen *et al.*, in view of Sallusto *et al.*, and further in view of Taylor *et al.* and Lutz *et al.* adds nothing to render obvious the immortalized dendritic cells of the invention as either previously or presently claimed.

In view of the amendments and remarks above, Applicants respectfully request the Examiner to reconsider and withdraw the various rejections of claims 23, 24, and 31-36 under 35 U.S.C. § 103 as being obvious over Cohen *et al.*, in view of Sallusto *et al.* and Inaba *et al.* Further, as Applicants believe that the claims have been demonstrated to be non-obvious over the primary references, it is further requested that the various rejections of the claims under 35 U.S.C. § 103 in view of each of the cited combinations of references also be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If

the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 17 December 2004 By: _____

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